Technical Information

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Ludiflash®

Excipient for fast-disintegrating oral dosage forms
Direct compressible formula

BASF
The Chemical Company

Pharma Ingredients & Services

Introduction

Ludiflash is a formulation for fast disintegrating solid oral dosage forms. The formulation of co-processed ingredients consists of three compendial ingredients: A sugar-alcohol, crospovidone and a polymer dispersion based on polyvinyl acetate. It is tailored to disintegrate readily on the tongue with a pleasant-creamy mouthfeel without a chalky or sandy sensation.

Ludiflash is suitable for direct compression manufacturing by simply blending the excipient with the active and a lubricant and is thus applicable for a very cost efficient production pathway.

Synonyms

none

Composition

Ludiflash consists of D-mannitol, crospovidone, polyvinyl acetate and small amounts of Povidone. Polyvinyl acetate is incorporated into the system as Kollicoat® SR 30 D, a polyvinyl acetate dispersion stabilized with Povidone.

CAS-No.

D-Mannitol	CAS-registry	69-65-8
Crospovidone (Kollidon® CL-SF)	CAS-registry	9003-39-8
Polyvinyl acetate (Kollicoat SR 30D)	CAS-registry	8003-20-7
Povidone (Kollidon 30)	CAS-registry	9003-39-8

Description

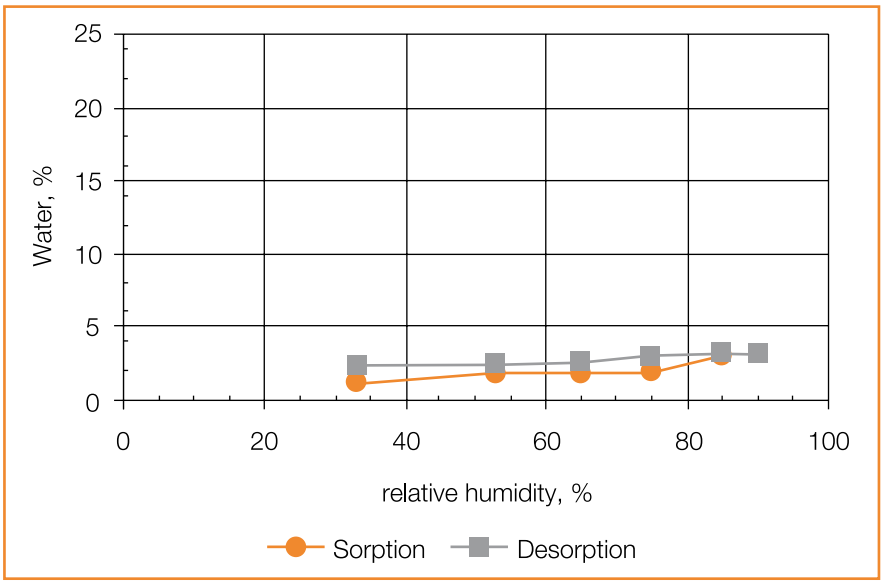
Ludiflash is a white to off-white powder with good flowability. The angle of repose was determined to be ~38°.

Specifications

See separate document: “Standard Specification (not for regulatory purposes)” available via the “BASF Pharma Solutions-homepage“.

Sorption isotherm

The product has a very low hygroscopicity, driven by the specific character of D-mannitol.



Sorption isotherm at 23°C

Solubility

Due to the content of crospovidone and polyvinyl acetate the product does not dissolve completely in water, nor is it entirely soluble in organic solvents.

Properties

As the product contains D-mannitol it can have a mild laxative effect.

The properties described in the following paragraph are considered to be typical values.

Particle size distribution (determined)	> 0.400 mm	max. 20%
	< 0.200 mm	max. 90%, min. 45%
	< 0.063 mm	max. 45%, min. 15%
Bulk density	0.40-0.52 g/ml	
pH (5% in water, partially dissolved)	5.5-6.5	

Packaging materials

Cardboard box with aluminum/PE inliner

General remarks

To achieve fast disintegrating solid oral dosage forms it is important to have tablets with high porosity which allows water to penetrate very fast. The careful control of the compression force is thus very important. 50 Mpa to 90 Mpa tabletting pressure, which corresponds to 3 – 6kN compression force for a 10mm tablet are most suitable.

Furthermore the control of humidity throughout tablet manufacturing and the use of vapor resistant packaging materials for the finished tablets should be considered.

Recommendations for Lubricants

Detailed tests revealed magnesium stearate and sodium stearyl fumarate to be appropriate lubricants for fast disintegrating formulations based on Ludiflash.

Recommendations for Taste Optimization

Tablets with optimum properties can be achieved when the following excipients are applied in the ranges given:

1. Sweeteners like aspartame in concentrations ranging from 0.3 to 0.7% or saccharine sodium in a concentration ranging from 0.05% to 0.1% were tested in various formulations and can be recommended.
2. To achieve an effervescent effect the combination of citric acid with sodium hydrogen carbonate can be formulated. Both compounds are applied in quantities of 0.5%.
3. To control the acidity of a tablet ascorbic acid or combinations of ascorbic acid and sodium ascorbate in concentrations, as well as citric acid can be used.
4. Vanilla flavor in a concentration of around 0.5% or L-Menthol in the range of 0.1% to 0.3% can be used with good tabletting results for aroma purposes.

Formulations

To demonstrate the basic properties of the exipient Ludiflash, placebo tablets were manufactured and checked for their properties.

Formulation 1

Ludiflash placebo formulation

Ludiflash	(BASF)	98%
Sodium stearyl fumarate	(JRS Pharma)	2%

Manufacturing
All components were blended in a Turbula blender for 10 minutes, passed through a sieve with a mesh size of 0.8mm and compressed into tablets

Tabletting equipment	Korsch XL 100 rotary press
Tablet size/shape	10mm, flat
Total tablet weight	300 mg

Even at very low compression forces (figure 1) in the range of 5 kN to 10 kN, which still allow very porous tablets, it is possible to achieve tablets sufficiently stable and showing a low friability. The disintegration time is in the range of less than 25 seconds when determined in a disintegration tester.

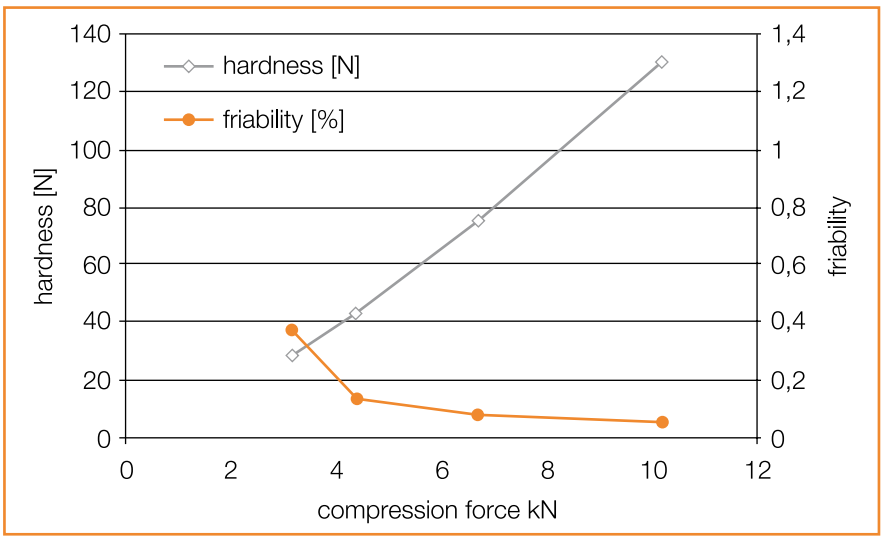


Figure 1. Hardness and friability as function of the compression force

In long time production runs the influence of tabletting speed on the uniformity of mass, hardness and friability was checked. For the tests rotation speeds of 20 rpm, 40 rpm and 60 rpm were used.

Figure 2 demonstrates that rotation speed has only little influence on disintegration time and hardness of the resulting tablets. The uniformity of mass (tested on 20 tablets) is well within the compendial ranges (figure 3).

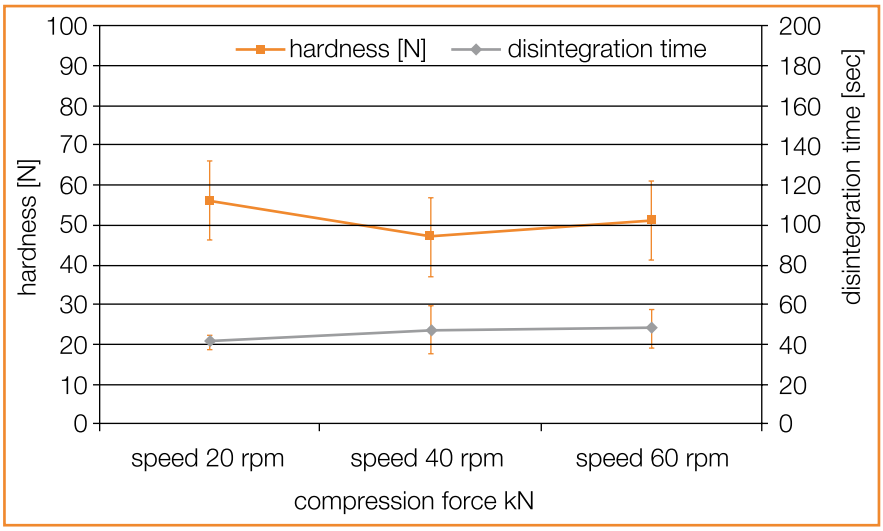


Figure 2. Hardness and disintegrations time as a function of rotation speed

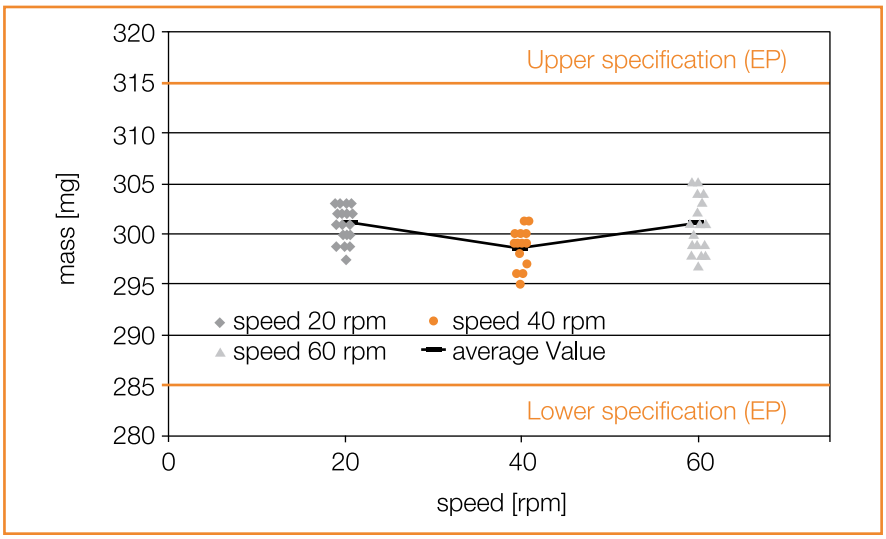


Figure 3. Uniformity of the tablet mass as a function of rotation speed

Formulation 2

Loperamide fast disintegrating tablet: 2mg

Loperamide HCl	(Select Chemie)	2.0 mg
Ludiflash	(BASF)	94.5 mg
Kollidon CL-SF	(BASF)	1.0 mg
Chocolate aroma	(Symrise)	1.5 mg
Sodium stearyl fumarate	(JRS Pharma)	1.0 mg
Total tablet weight		100.0 mg

Manufacturing
All components were blended in a Turbula free fall blender for 10 minutes, passed through a sieve with a mesh size of 0.8mm and compressed into tablets at 3.8 kN.

Tablet Properties

Tablet weight	100.0 mg
Form	7 mm concave
Hardness	32 N
Friability	0.09%
Disintegration time (phosphate buffer pH 7.2)	11 s
Dissolution (0.01 N HCl/100 rpm)	94.7% (30 min)
Taste	quickly disintegrating in the oral cavity, slightly bitter, chocolate taste, very smooth mouthfeeling

The content uniformity (figure 4) and the dissolution profile (figure 5) of the Loperamide tablets are shown in the following figures:

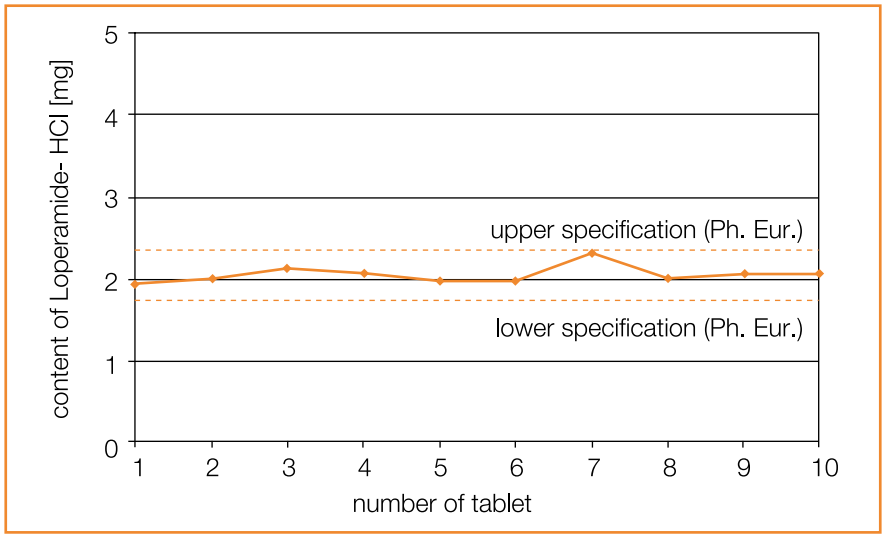


Figure 4. Content uniformity of Loperamide Tablets (2 mg)

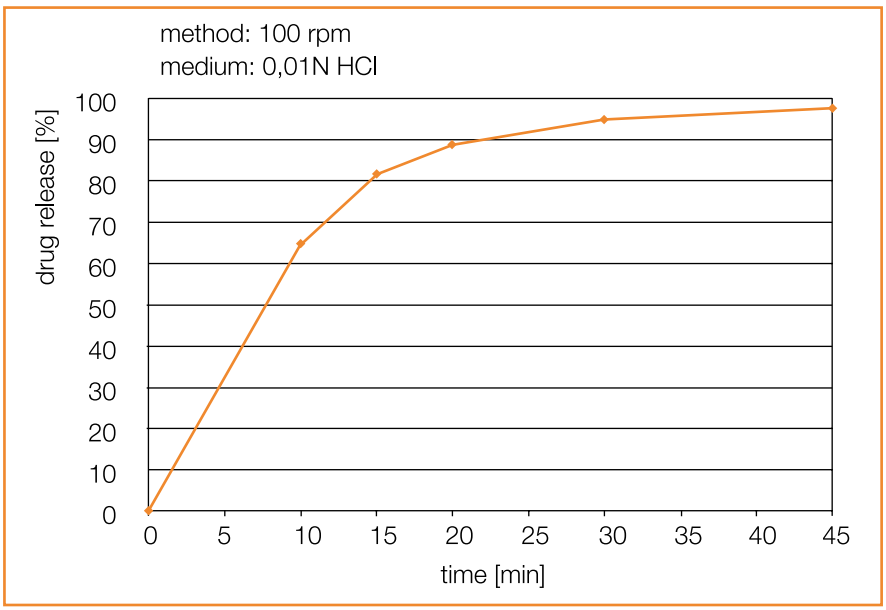


Figure 5. Dissolution profile of Loperamide tablets (2 mg)

Formulation 3

Loratadine fast disintegrating tablet: 10mg

I	Loratadine	(Select Chemie)	10.00 mg
	Ludiflash	(BASF)	39.70 mg
	Saccharin-Sodium	(Merck)	0.26 mg
II	Kollidon 25	BASF)	1.02 mg
III	Ludiflash	(BASF)	142.02 mg
	Peppermint-aroma	(Bell Flavours & Fragrances)	3.00 mg
	Magnesium stearate	(Baerlocher)	4.00 mg
	Total tablet weight		200.00 mg

Manufacturing

The components of I were granulated with a 6.5% aqueous solution of II in a Glatt GPC G3 fluid bed granulator (atomizing pressure 0.5bar, inlet air temperature 45-50°C, outlet air temperature 30°C). The resulting granules were blended with III in a Turbula blender for 10min, passed through a 0.8mm sieve and compressed into tablets at 2.8kN.

Tablet properties

Tablet weight	200.0 mg
Tablet form	8 mm, flat
Hardness	37.0 N
Friability	0.25%
Disintegration time (phosphate buffer pH 7.2)	38 s
Dissolution (0.1 N HCl/50 rpm)	98.8% (10 min)

The content uniformity and the dissolution profile of the Loratadine tablets are shown in the following figures:

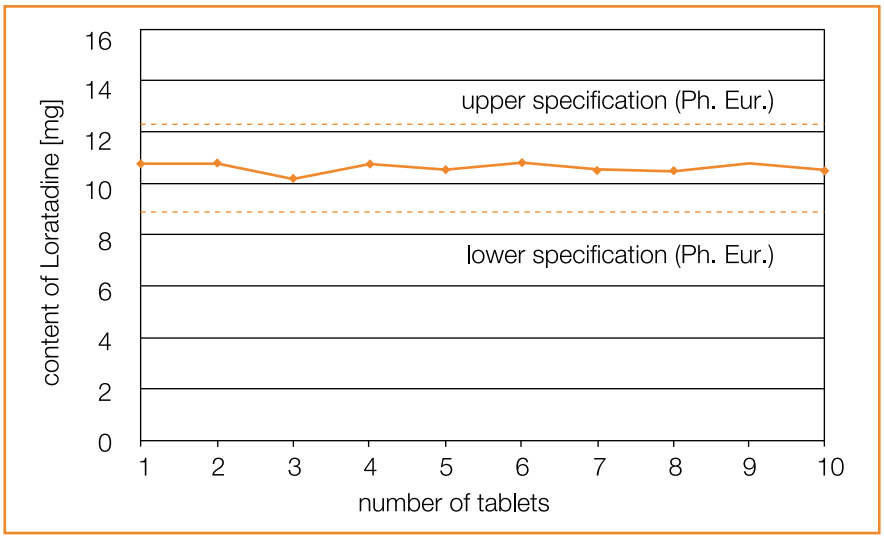


Figure 6: Content uniformity of Loratadine tablets (10 mg)

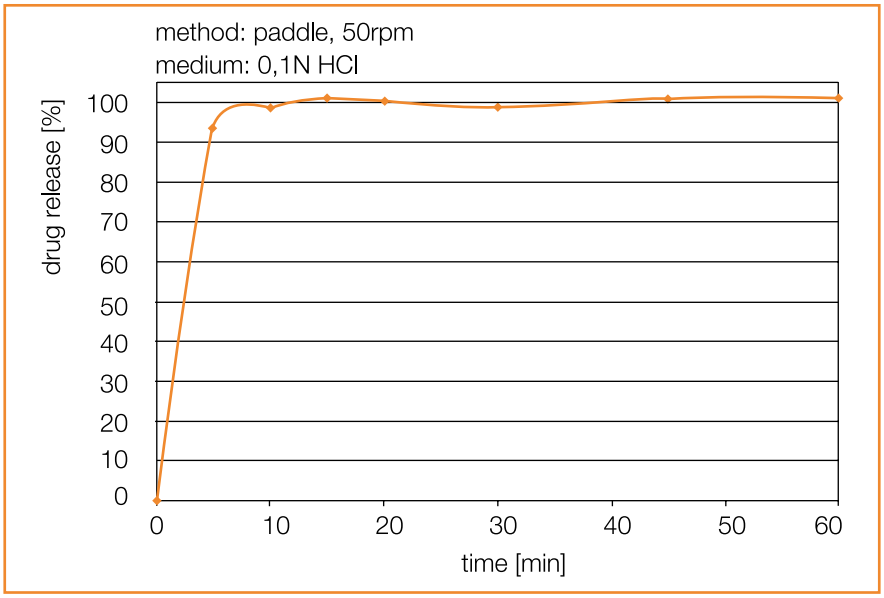


Figure 7: Dissolution profile of Loratadine tablets (10 mg)

Formulation 4

Famotidine fast disintegration tablet: 20 mg

Famotidine	(Various sources)	20.0 mg
Ludiflash	(BASF)	267.1 mg
Aerosil® 200	(Degussa)	3.0 mg
L-Menthol	(Symrise)	0.9 mg
Aspartame	(Ajinomoto)	4.5 mg
Sodium stearyl fumarate	(JRS Pharma)	4.5 mg
Total tablet weight		300.0 mg

Manufacturing

All components were blended in a Turbula free fall blender for 10 minutes, passed through a sieve with a mesh size of 0.8 mm and compressed into tablets at 0.8 ton/cm^2, corresponding to ~10 kN for a 10 mm tablet.

Tablet properties

Tablet weight	300 mg
Tablet form	10 mm, 10 R
Rotation speed	40 rpm
Hardness	51 N
Friability	<0.2%
Disintegration time (phosphate buffer pH 7.2)	27 s
Dissolution (N=10); 0.05 mol/L acetic acid/Na-acetate buffer pH 4.0, 50 rpm	98.8% (10 min)

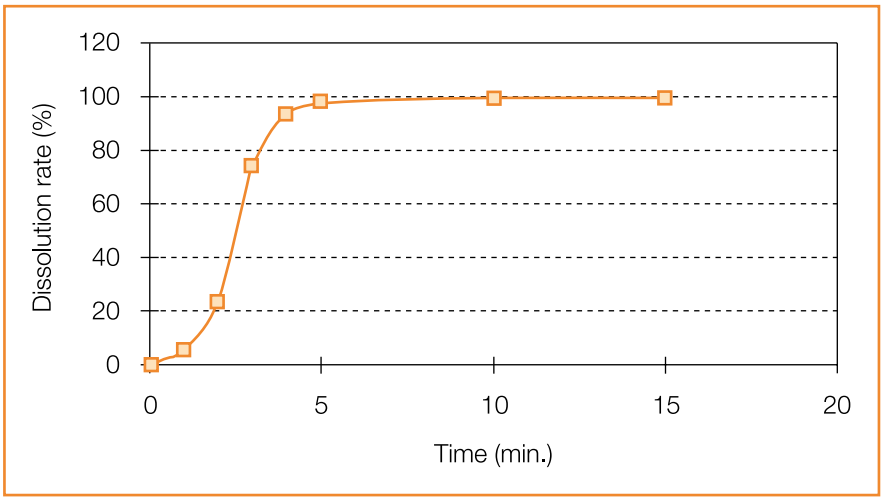


Figure 8. Dissolution of Famotidine

Content uniformity (N=10)
Ave.= 100.5%
Max= 101.5%
Min = 97.4%
SD = 1.2

Formulation 5

Cetirizine fast disintegration tablet: 5 mg

Cetirizine	(Daito)	5.0 mg
Ludiflash	(BASF)	163.4 mg
Aerosil 200	(Degussa)	2.0 mg
Avicel® PH 101	(FMC)	20.0 mg
Grapefruit powder	(Symrise)	2.0 mg
L-Menthol	(Takasago International)	0.6 mg
Aspartame	(Ajinomoto)	4.0 mg
Sodium stearyl fumarate	(JRS Pharma)	3.0 mg
Total tablet weight		200.0 mg

Manufacturing

All components were blended in a Turbula free fall blender for 10 minutes, passed through a sieve with a mesh size of 0.8 mm and compressed into tablets at 0.8 ton/cm^2, corresponding to ~14 kN for a 8.5 mm tablet.

Tablet properties

Tablet weight	200 mg
Tablet form	8.5 mm, 12 R
Rotation speed	40 rpm
Hardness	51 N
Friability	<0.2%
Disintegration time (phosphate buffer pH 7.2)	32 s
Dissolution(N=10); water, 50 rpm	98.8% (10 min)

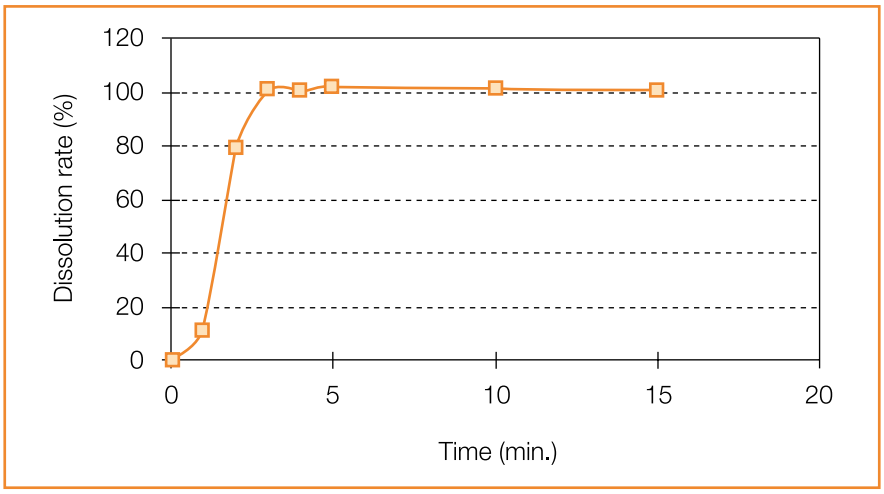


Figure 9. Dissolution of Cetirizine

Content uniformity (N=10)
Ave. = 101.4%
Max = 102.7%
Min = 98.6%
SD = 1.6

PBG-Number	10708891
PRD-Number	30280988
Packaging	20 kg, cardboard box with a liner compounded of aluminium/PE Article number: 56513304 1 kg, PE-bottle with screw-head Article number: 53269227
Stability	Based on presently available stability data the product has a retest period of 24 months in the unopened original container.
Safety data sheet	Safety data sheets are available on request and are sent with every shipping.
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